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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,816	04/05/2000	XIAOMAO LI	1038-1003-MI	5549

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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/10/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/462,816	Applicant(s) LI ET AL.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,13-23,27-34 and 39-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13-23,27-34 and 39-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 April 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Final Rejection

Claims 1-9, 13-23, 27-34, and 39-42 are pending examination.

Applicants amendments to claims 1, 3, 13-15, 17, 27, 28, 30, 40, cancellation of claims 10-12, 24-26, 35-38, and 43-48, amendment to specification (priority status), and traversal in paper no. 12 filed on 2/4/02 is acknowledged and considered by examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants' argue that the rejection for claims 1-29, 36-38, and 40-42 under 112 first written description because: the amendment to claims 1, 15, 30, and 40 to incorporate human cytomegalovirus Intron A as the second nucleotide sequence located between the first nucleotide sequence and said promoter sequence and the cancellation of claims 36-38 comprising an immunoprotection enhancing sequence. See pages 5-6

Applicants' traversal is acknowledged and is found persuasive. The rejections under 112 first written description for claims 1-29, 36-38, and 40-42 are withdrawn.

Claims 1-9, 13-23, 27-34, and 39-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling 1) An immunogenic composition comprising a plasmid that will not replicate, wherein the plasmid comprises: a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment thereof, a

cytomegalovirus promoter sequence operatively linked to the first nucleotide sequence for expression of the RSV G protein or fragment thereof, and a second nucleotide sequence encoding the human cytomegalovirus Intron A located between the first nucleotide sequence and the promoter sequence to increase expression of the RSV G protein or fragment thereof; 2) A method of stimulating an immune response in a mammal using an effective amount of the composition of 1; 3) A method for using a gene encoding a RSV G protein or a fragment thereof to produce an immunogenic composition, comprising the following steps: a) isolating a gene encoding a RSV G protein or a RSV G fragment thereof; b) operatively linked the gene or fragment thereof to an cytomegalovirus promoter sequence to produce a plasmid vector that will not replicate when introduced into a mammal; and c) introducing a second nucleotide sequence encoding the human cytomegalovirus Intron A into the plasmid from step b) between the first nucleotide sequence and the promoter sequence to increase expression of the RSV G protein or fragment thereof, thereby producing an immunogenic composition that generates antibodies that specifically react with RSV G protein; 4) A method of administering the composition from step c) of 3 to a mammal, to stimulate an immune response in said mammal, and the as-filed specification does not reasonably provide enablement for any other embodiment as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention encompasses an immunogenic composition comprising a plasmid vector comprising a first nucleotide sequence encoding a RSV G protein or fragment thereof and a control sequence directing expression of said RSV G protein when introduced into host to produce an immune response to said RSV G protein; and operatively linking said first nucleotide sequence to a second nucleotide sequence to increase expression of said RSV G protein in vivo from the vector in the host, and a method of producing a vaccine for protection (encompasses partial/complete protection) or prevention (total protection) of a host against a disease caused by infection with RSV, including infection by a pathogen (e.g. viruses, bacteria, fungus, etc.). Furthermore, the claimed invention includes a method of immunizing a host against disease caused by infection with RSV by using the immunogenic composition described above, wherein said a balance Th1/Th2 immune response. The invention lies in the field of producing an immunogenic composition or vaccine using a replicant defective vector encoding a viral protein (RSV G protein).

The state of the art exemplified by Gurunathan et al. indicates that the goal of developing effective vaccines for a particular disease depends on several factors:

1) Identification of a conserved antigen capable of inducing protection is an outbred population.

2) Design vaccines that can induce an appropriate qualitative and quantitative immune response.

3) Some diseases require different types of immune responses for effective primary and memory immunity (*J Immunol*, Vol. 161(9), pg. 4563, November 1998).

In addition, major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered

2) The route and time course of administration, the sites of administration, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

3) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method (Anderson et al., *Nature*, Vol. 392, pp. 25-30, April 1998).

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the subject being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson indicates that the state of the art before 1998, and teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in a subject is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma et al., *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Thus, in view of the state of the art, producing an immunogenic composition or vaccine using a plasmid vector encoding a nucleotide sequence is considered unpredictable.

The application provides sufficient guidance and/or factual evidence showing 1) immunization of BALB/c mice with live RSV intranasally resulted in a balance cytokine profile; 2) immunization in BALB/c mice with PXL5 or PXL6 (vectors encoding a gene encoding a full length membrane attached form of the RSV G protein and containing the CMV intron A sequence or gene encoding a secreted form of the RSV G protein lacking the trans-membrane domain and the CMV intron A sequence as well as a nucleotide sequence encoding a signal peptide of the human tissue plasminogen activator, respectively) via either the i.m. or intradermal (i.d.) route, which gave rise to a balanced cytokine profile (page 30, lines 5-35).

However, the as-filed specification does not provide sufficient guidance and/or factual evidence demonstrating a reasonable correlation between the disclosure including its exemplified examples and the subject matter being sought in the claims wherein an immunogenic composition comprising a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment, a promoter sequence operatively coupled to said first nucleotide sequence for expression of said RSV G protein in the host, and a second nucleotide sequence located between said first nucleotide sequence and said promoter sequence to increase expression of said RSV G protein in vivo from said vector in host can be used to stimulate a vaccine effect (e.g. encompassing treatment or prevention); against any diseased or infectious antigen, particularly given all of the reasons set forth above. In addition, the as-filed specification does not provide sufficient guidance for one skilled in the art how to induce a balanced Th1/Th2 immune response in any host using an immunogenic composition comprising a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment thereof, a promoter sequence operatively coupled to said first nucleotide

sequence for expression of said RSV G protein in the host, and a second nucleotide sequence located between said first nucleotide sequence and said promoter sequence to increase expression of said RSV G protein in vivo from said plasmid vector in any host other than the experimental mice. Thus, it is not apparent how one skilled in the art determines, without undue experimentation, which of the disclosed DNA complexes claimed in the disclosure generate a treatment (encompasses partial/complete protection) or prevention (total protection) in any nucleic acid therapy methods as contemplated by the as-filed specification, particularly given the unpredictability of nucleic acid therapy as a whole and/or the doubts expressed in the art of record.

In addition with respect to claims encompassing a method of immunizing against RSV and/or a method of producing a vaccine in any host for treatment (encompasses partial/complete protection) or prevention (total protection) including any host (*e.g.* bird, fish, snake, mammal, etc.) wherein any administration route including injection route is contemplated. The applicants provide sufficient guidance for intramuscular administration of the immunogenic composition in the 1-4, listed above; however, the as-filed specification does not provide sufficient guidance for any other route of administering the immunogenic composition.

In addition to the doubts expressed in Anderson and Verma, the state of art exemplified by McCluskie et al. (*Molecular Medicine*, 5, pp. 287-300, 1999) teach that "the realization that results in mice often do not predict the situation in humans has also led to a large number of DNA vaccine studies in non-human primates", that "IM injection of plasmid DNA vaccines, while highly immunogenic in mice...was found only to be relatively so in chimpanzees..., and especially not all in Aotus monkeys"' and that "it is probably safe to say that any vaccine that

works in a human will work in a mouse, but note necessarily vice-versa" (page 296, column 2, second and third paragraphs). In addition, McCluskie et al. teach that "although non-human primate models are frequently used for development and testing of human vaccines, it is not clear how predicative they will be in the case of DNA vaccines where efficacy, by virtue of the requirement first to transfect cells and express the antigen, relies on many factors other than immunological reponses to the antigen" (page 297, column 1).

Thus, it is not apparent as how one skilled in the art reasonably extrapolates, without undue experimentation, from the scope of vertebrate to the full scope of the claimed invention that would generate a treatment (encompasses partial/complete protection) and/or prevention (total protection) in any subject against any disease. Even if a protective response has been shown in mice using the experimental mice, it is not apparent as to how the mouse model wherein it is reasonably extrapolated to the full scope of the claimed invention, encompassing any host (*e.g.*, snake, bird, fish, mammal, etc.) particularly given that there is no vaccine generation evidence showing that the mice model is a general phenomenon, and given the doubts expressed in the art of record.

With respect to vaccination methods encompassing routes of administration, e.g., intranasally and intramuscular, the state of the art exemplified by McCluskie teaches that the route of delivery of the DNA vaccine can have an impact on the efficiency of transfection as well as the types and location of cells transfected, and thus potentially on the nature of the immune response (pg. 295). In addition, McCluskie teaches that many different routes have been shown to be effective for DNA delivery in mice; however, few studies have compared responses obtained with different routes using the same antigen-expressing DNA, dose, and immunization

schedule. There have been even fewer studies to compare routes of administration in non-human primates (pg. 295).

The as-filed specification, applicants' traversal and claims coupled with the state of the art at the time the invention was made only provide sufficient guidance and/or factual evidence to reasonably enable the claimed invention 1-4, listed above. One would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the application's disclosure, the unpredictability of gene therapy (Anderson, *Nature*, Vol. 392, pp.25-30, 1998) and developing effective vaccines (Gurunathan et al., *J Immunol*, Vol. 161(9), pg. 4536, 1998) encompassing any vertebrate subject including any mammal for a protective effect and/or treatment McCluskie et al. (*Molecular Medicine*, 5, pp. 287-300, 1999). In addition, the presence of a working example as provided in the specification does not extrapolate to the full scope of the claimed invention, particularly given that there is no evidence that the mice model is a general phenomenon.

Applicants' argue that claims 1-42 as they remain in the application are enabled under 112 first and the rejection should be withdrawn because: Claims 1, 15, 30, and 40 have been amended to recite the subject matter that examiner considers to be enabled, in particular the identity of the promoter and the second nucleotide sequence, The cancellation of claims 10-12, 24-26, 35-39. See pages 6-7.

The applicants' traversal is acknowledged and is not found persuasive because as stated the above the disclosure is only enabled for 1-4 listed above. Furthermore, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed

invention based on the application's disclosure, the unpredictability of gene therapy (Anderson, *Nature*, Vol. 392, pp.25-30, 1998) and developing effective vaccines (Gurunathan et al., *J Immunol*, Vol. 161(9), pg. 4536, 1998) encompassing any vertebrate subject including any mammal for a protective effect and/or treatment. In addition, the presence of a working example as provided in the specification do not reasonably extrapolate to the full scope of the claimed invention, particularly given that there is no evidence that the mice model is a general phenomenon. Therefore, the rejections under 112 first paragraph remain and the claimed invention is only enabled for 1-4 listed above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Applicants' traverse that the rejections for claims 1, 3, 15, 17, 36-38, and 40 under 112 second should be withdrawn because: The amendment to claims 1, 3, 15, 17, and 40 and the cancellation of claims 36-38. See pages 7-8.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In view of the applicants' traversal (see pages 8-9) and the amendment to claims the rejections under 102(b) are withdrawn.

Claim Rejections - 35 USC § 103

The rejection of claims under 103(a) is withdrawn in view of applicant's amendment and cancellation of the claims and in view of the applicants' traversal. See pages 9-10.

However, in view of the amended claims, a new ground of rejections under 103(a) follows:

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5-7, 15-16, 19-20, and 30-34 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Olmsted et al. (1989, J. Virol., Vol. 63 (1), 411-420) and Simard et al. (Antiviral Research, Vol. 28, pp. 303-315, 1995) in view of Johnson et al. (1987, Proc. Natl. Acad. Sci., Vol. 84, 5625-5629), Wagener et al. (1996, J. Biotech., Vol. 44, 59-65), Norman et al. (June, 1997, Vol. 15 (8), 801-803), and Haddad et al. (July, 1997, Vol. 18, 193-202). Olmsted teaches recombinant vaccinia viruses, which encode either full length or truncated versions of the human RSV G protein, and demonstrates that intranasal administration to rats with the recombinant G protein encoding vaccinia viruses resulted in significant anti-RSV G protein antibody titers (Olmsted et al., page 412, Figure 1, and page 417, Table 1). Olmsted et al. further teaches that the G protein from three strains of RSV, including the Long strain has been sequenced (Olmsted et al., page 411, column 2). Simard also teaches recombinant vaccinia viruses comprising an RSV G protein. Specifically, Simard teaches a fragment corresponding to amino acids 124-203 of the RSV G protein of the Long strain which lacks the trans-membrane region and sequences upstream (Simard et al., page 311, paragraph 2). Simard et al. also teaches that administration to mice with the recombinant plasmid generated significant anti-RSV antibody titers (Simard et al., page310, Table 1). It is further noted that Simard comments that the vaccinia virus is not expected to become a suitable vector for the development of human vaccines (Simard et al., page 313, paragraph 2). Johnson supplements both Olmsted, and Simard

by providing the amino acid sequence of the G protein derived from the Long strain of RSV which is 99.1% identical to the nucleic acid sequence encoding applicants SEQ ID NO: 2 (Johnson et al., page 5627, Figure 2). However, Olmsted and Simard differ from the instant invention in that they utilize replicating vectors i.e. vaccinia virus.

However, at the time the invention was made, Simard suggests that the vaccinia virus is not the vector of choice for use in humans. Wagener supplements Olmsted and Simard by teaching that immunogenic compositions may be safer than live attenuated viruses and that immunogenic compositions comprising a plasmid can be used to induce an immune response similar in scope to attenuated viruses (Wagener et al., page 60, paragraph 2). More specifically, Wagener teaches that administration to mice with a non-replicating plasmid vector encoding a CMV promoter and CMV intron A operatively linked to the tissue plasminogen activator (tPA) leader sequence and the SIV gp130 antigen resulted in significant titers of anti-SIV antibodies (Wagener et al., pages 62- 63, and Figures 2+ 3). Norman supports Wagener by teaching that the optimized plasmid vector for gene expression and delivery *in vivo* includes a CMV promoter and enhancer and the CMV IE intron A (Norman et al., page 801, abstract). Haddad further supports Wagener by teaching that the addition of the tPA signal sequence is warranted in order to prevent retention of peptides in the cytoplasm and to ensure proper glycosylation in the ER (Haddad et al., page 201, paragraph, 3).

Therefore, in view of the optimal nature of the plasmid vector taught by Wagener et al. which includes the CMV promoter, CMV intron A, and the tPA signal sequence as taught by Norman and Haddad, and in view of the teachings of Wagener which support the use of plasmid vector over attenuated viral vectors to induce antigen specific antibodies, it would have been

prima facie obvious to the skilled artisan to use the plasmid vector taught by Wagener to express the RSV G proteins taught by Olmsted, Johnson, or Simard in order to generate anti-RSV antibody responses *in vivo*. Further based on the well known techniques of molecular biology and the teachings of Olmsted and Simard that the RSV G protein are produced *in vivo*, the skilled artisan would have had a reasonable expectation of success in making a plasmid encoding CMV promoter, CMV intron A, and the tPA signal sequence and an RSV G protein and using said plasmid to produce an immunogenic composition used to produce antibodies that specifically react with RSV G protein in a mammal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

The applicants argue that the previous rejection of the claims did not include using a plasmid vector because Stott teaches a vaccinia vector and provides no evidence for using a plasmid vector. Therefore, the applicant argues that the amended claims should be free of the art of record. However, following applicant's amendment to claims, the examiner was able to determine that using a plasmid vector instead of a vaccinia vector was taught by prior art and that a new 103 rejections is applicable as set forth above.

No claims are allowed.

Note: Another 103(a) rejection can be applied to the amended claims as set forth below.

Claims 1-2, 5-7, 15-16, 19-20, and 30-34 are newly rejected under 35 U.S.C. 103(a) as being Stott et al. (Journal of Virology, Vol. 60, pp. 607-613, 1986) and Johnson et al. (1987,

Proc. Natl. Acad. Sci., Vol. 84, 5625-5629) taken with Simard et al. (Antiviral Research, Vol. 28, pp. 303-315, 1995), Wagener et al. (1996, J. Biotech., Vol. 44, 59-65) and Haddad et al. (July, 1997, Vol. 18, 193-202) in further view of Herrmann et al. (Applicants' IDS, US patent 5,620,896, 1997). Stott displays that RSV G protein expressed from a recombinant vector can produced antibodies specific for the RSV G protein (abstract). Stott produced a plasmid containing a complete cDNA copy of the RSV G gene (page 607). Stott further teaches that the G protein expressed from the recombinant vector induced antibodies in rabbits (page 607). Johnson supplements Stott by providing the amino acid sequence of the RSV G protein derived from the Long strain of RSV which is 99.1% identical to the nucleic acid sequence encoding applicants SEQ ID NO: 2 (Johnson et al., page 5627, Figure 2). However, Stott and Johnson differ from the instant invention that Stott utilized a vaccinia virus vector.

However, at the time the invention was made, Simard suggests that the vaccinia virus is not the vector of choice for use in humans. Wagener supplements Simard by teaching that immunogenic compositions may be safer than live attenuated virus vaccines and that immunogenic compositions induce immune responses similar in scope to attenuated viruses (Wagener et al., page 60, paragraph 2). More specifically, Wagener teaches that administration to mice with a non-replicating plasmid vector encoding a CMV promoter and CMV intron A operatively linked to the tissue plasminogen activator (tPA) leader sequence and the SIV gp130 antigen resulted in significant titers of anti-SIV antibodies (Wagener et al., pages 62- 63, and Figures 2+ 3). Haddad further supports Wagener by teaching that the addition of the tPA signal sequence is warranted in order to prevent retention of peptides in the cytoplasm and to ensure proper glycosylation in the ER (Haddad et al., page 201, paragraph, 3). Furthermore, Herrmann

provides a control plasmid pCMVIA, a bacterial plasmid that includes SV40 replication origin, the CMV promoter, Intron A and a bovine growth hormone gene that provides a polyadenylation signal (column 5, lines 56-63). Furthermore, Herrmann uses the plasmid, wherein the promoter is operably linked to a nucleotide sequence encoding a rotavirus polypeptide wherein said rotavirus polypeptide is expressed in a cell of a mammal with said plasmid vector (column 27, lines 39-45).

It would have been *prima facie* obvious for a person of ordinary skill in the art at the time the invention was made to modify the teaching of Stott and Johnson taken with Simard, Wagener, and Haddad in further view of Herrmann to produce an immunogenic composition comprising a RSV G protein to produce an immune response in a mammal. One of ordinary skill in the art would have been motivated to produce this composition since it would facilitate the expression of antibodies specific for the RSV G protein when administered to a mammal.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

In addition, the Stott reference is dated 1986 and not 1997 as indicated in applicants' traversal, which is ten years before the applicants filing date, thus the Stott reference is considered a 102(b) reference since it was published 9 years before the applicants filed their application.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, primary examiner, Dave Nguyen can be reached at (703) 305-2024.

If attempts to reach the primary examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635
4/5/02

DAVE T. NGUYEN
PRIMARY EXAMINER